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FILE LAST UPDATED: 27 Feb 2006  (20060227/ED)

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=> s 99-31-0/rn or 554-95-0/rn or 535-87-5/rn
           368 99-31-0
            13 99-31-0D
           357 99-31-0/RN
                 (99-31-0 (NOTL) 99-31-0D )
          1038 554-95-0
           108 554-95-0D
           951 554-95-0/RN
                 (554-95-0 (NOTL) 554-95-0D )
           374 535-87-5
            35 535-87-5D
           343 535-87-5/RN
                 (535-87-5 (NOTL) 535-87-5D )
L17       1566 99-31-0/RN OR 554-95-0/RN OR 535-87-5/RN

=> s 108-72-5/rn
           178 108-72-5
            13 108-72-5D
L18        167 108-72-5/RN
                 (108-72-5 (NOTL) 108-72-5D )

=> s L17 or L18
L19       1670 L17 OR L18

=> s biotin or norbiotin or homobiotin or oxybiotin or iminobiotin or desthiobiotin
or diaminobiotin
          28899 BIOTIN
            110 BIOTINS
          28909 BIOTIN
                 (BIOTIN OR BIOTINS)
             32 NORBIOTIN
             48 HOMOBIOTIN
             73 OXYBIOTIN
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             1 OXYBIOTINS
            73 OXYBIOTIN
                 (OXYBIOTIN OR OXYBIOTINS)
           144 IMINOBIOTIN
           244 DESTHIOBIOTIN
             1 DESTHIOBIOTINS
           245 DESTHIOBIOTIN
                 (DESTHIOBIOTIN OR DESTHIOBIOTINS)
            31 DIAMINOBIOTIN
L20      29004 BIOTIN OR NORBIOTIN OR HOMOBIOTIN OR OXYBIOTIN OR IMINOBIOTIN
               OR DESTHIOBIOTIN OR DIAMINOBIOTIN

=> s L19 and L20
L21         16 L19 AND L20

=> d L21 1 ibib abs

L21  ANSWER 1 OF 16  CAPLUS  COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER:        2004:349779  CAPLUS
DOCUMENT NUMBER:         141:102297
TITLE:                   Biotin Reagents in Antibody Pretargeting. 6.
                         Synthesis and in Vivo Evaluation of Astatinated and
                         Radioiodinated Aryl- and nido-Carboranyl-
                         biotin Derivatives
AUTHOR(S):               Wilbur, D. Scott; Hamlin, Donald K.; Chyan, Ming-Kuan;
                         Kegley, Brian B.; Quinn, Janna; Vessella, Robert L.
CORPORATE SOURCE:        Departments of Radiation Oncology and Urology,
                         University of Washington, Seattle, WA, 98195, USA
SOURCE:                  Bioconjugate Chemistry (2004), 15(3), 601-616
                         CODEN: BCCHES; ISSN: 1043-1802
PUBLISHER:               American Chemical Society
DOCUMENT TYPE:           Journal
LANGUAGE:                English
AB   An investigation has been conducted to prepare and evaluate several
     radiohalogenated biotin derivs. as part of our studies to
     develop reagents for carrying 211At in cancer pretargeting protocols. The
     primary goal of the investigation was to determine the in vivo stability and
     distribution properties of astatinated biotin derivs. In addition
     to astatination, the biotin derivs. were radioiodinated for in
     vitro and in vivo comparison. Biodistributions were conducted in athymic
     mice, with sacrifice times of 1, 4, and 24 h to correspond to 9%, 32%, and
     90% of 211At decay (t1/2 = 7.21 h). In the investigation, two
     biotin derivs., 1a and 2a, were synthesized which had structures
     that contain a biotin moiety, a biotinidase-blocking moiety, an
     ether linker moiety, and an aryl stannane moiety for radiohalogenation.
     Biotin derivs. 1a and 2a were radiolabeled with 125/131I to give
     [125/131I]1b or [125I]2b and with 211At to give [211At]1c or [211At]2c.
     In vivo studies demonstrated that co-injected [125I]2b and [131I]1b had
     very similar tissue distributions in athymic mice. Co-injection of
     [211At]2c and [125I]2b provided data that indicated that rapid
     deastatination occurred in vivo. A second set of biotin
     derivs., 3a, 4a, and 5a, were synthesized which had structures that
     contain a biotin moiety, a biotinidase-blocking moiety, and an
     anionic nido-carborane moiety for radiohalogenation. The biotin
     derivs. 4a and 5a contained an aryl moiety not present in 3a, and 5a had a
     trialkylamine functionality not present in 3a or 4a. Biotin
     derivative 3a was radioiodinated, but was not further investigated.
     Biotin derivs. 4a and 5a were radiolabeled with 211At and 125I to
     produce [125I]4b/[211At]4c and [125I]5b/[211At]5c. Comparison of [125I]4b
     and (sep.) [125I]5b with [131I]1b showed that the nido-carborane containing
     biotin derivs. were retained in blood and tissue more than the
     aryl iodide derivative In vivo evaluations of [211At]4c/[125I]4b and (sep.)
     [211At]5c/[125I]5b indicated that some deastatination occurred in these
     compds., but it was much less than observed for the aryl derivative [211At]2c.
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While the nido-carborane containing **biotin** derivs. provide a significant improvement in astatine stability over **biotin** derivs. previously studied, addnl. derivs. need to be prepared and studied to further improve the in vivo stability and blood/tissue clearance of these compds.

REFERENCE COUNT: 57 THERE ARE 57 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> d L21 2-16 ibib abs

L21 ANSWER 2 OF 16 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2002:523951 CAPLUS
DOCUMENT NUMBER: 137:228855
TITLE: Trifunctional conjugation reagents. Reagents that contain a **biotin** and a radiometal chelation moiety for application to extracorporeal affinity adsorption of radiolabeled antibodies
AUTHOR(S): Wilbur, D. Scott; Chyan, Ming-Kuan; Hamlin, Donald K.; Kegley, Brian B.; Nilsson, Rune; Sandberg, Bengt E. B.; Brechbiel, Martin
CORPORATE SOURCE: Department of Radiation Oncology, University of Washington, Seattle, WA, 98195, USA
SOURCE: Bioconjugate Chemistry (2002), 13(5), 1079-1092
CODEN: BCCHES; ISSN: 1043-1802
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English

AB A method of removing radiolabeled monoclonal antibodies (mAbs) from blood using a device external to the body, termed extracorporeal affinity-adsorption (EAA), is being evaluated as a means of decreasing irradiation of noncancerous tissues in therapy protocols. The EAA device uses an avidin column to capture biotinylated-radiolabeled mAbs from circulated blood. In this investigation, three trifunctional reagents have been developed to minimize the potential deleterious effect on antigen binding brought about by the combination of radiolabeling and biotinylation of mAbs required in the EAA approach. The studies focused on radiolabeling with 111In and 90Y, so the chelates CHX-A''-DTPA and DOTA, which form stable attachments to these radionuclides, were incorporated in the trifunctional reagents. The first trifunctional reagent prepared did not incorporate a group to block the **biotin** cleaving enzyme biotinidase, but the two subsequent reagents coupled aspartic acid to the **biotin** carboxylate for that purpose. All three reagents used 4,7,10-trioxa-1,13-tridecanediamine as water-soluble spacers between an aminoisophthalate core and the **biotin** or chelation group. The mAb conjugates were radioiodinated to evaluate cell binding as a function of substitution. Radioiodination was used so that a direct comparison with unmodified mAb could be made. Evaluation of the number of conjugates per antibody vs. cell binding immunoreactivities indicated that minimizing the number of conjugates was best. Interestingly, a decrease of radioiodination yield as a function of the number of isothiocyanate containing conjugates per mAb was noted. The decreased yields were presumably due to the presence of thiourea functionality formed in the conjugation reaction. Radiolabeling with 111In and 90Y was facile at room temperature for conjugates containing the CHX-A'', but elevated temperature (e.g., 45°) was required to obtain good yields with the DOTA chelate. Stability of 90Y labeled mAb in serum, and when challenged with 10 mM EDTA, was high. However, challenging the 90Y labeled mAb with 10 mM DTPA demonstrated high stability for the DOTA containing conjugate, but low stability for the CHX-A'' containing conjugate.

Thus, the choice between these two chelating moieties might be made on requirements for facile and gentle labeling vs. very high in vivo stability. Application of the trifunctional biotinylation reagents to the blood clearance of labeled antibodies in EAA is under investigation. The

new reagents may also be useful for other applications.
REFERENCE COUNT: 62 THERE ARE 62 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L21 ANSWER 3 OF 16 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2002:319261 CAPLUS
DOCUMENT NUMBER: 137:59601
TITLE: A Streptavidin-**Biotin** Binding System That Minimizes Blocking by Endogenous **Biotin**
AUTHOR(S): Hamblett, Kevin J.; Kegley, Brian B.; Hamlin, Don K.; Chyan, Ming-Kuan; Hyre, David E.; Press, Oliver W.; Wilbur, D. Scott; Stayton, Patrick S.
CORPORATE SOURCE: Departments of Bioengineering, Medicine, and Radiation Oncology, University of Washington, Seattle, WA, 98195, USA
SOURCE: Bioconjugate Chemistry (2002), 13(3), 588-598
CODEN: BCCHES; ISSN: 1043-1802
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Pretargeted radioimmunotherapy specifically targets radiation to tumors using antibody-streptavidin conjugates followed by radiolabeled **biotin**. A potential barrier to this cancer therapy is the presence of endogenous **biotin** in serum, which can block the **biotin**-binding sites of the antibody-streptavidin conjugate before the administration of radiolabeled **biotin**. Serum-derived **biotin** can also be problematic in clin. diagnostic applications. Due to the extremely slow dissociation of the **biotin**-streptavidin complex, this endogenous **biotin** can irreversibly block the **biotin**-binding sites of streptavidin and reduce therapeutic efficacy, as well as reduce sensitivity in diagnostic assays. We tested a streptavidin mutant (SAv-Y43A), which has a 67-fold lower affinity for **biotin** than wild type streptavidin, and three bivalent bis-**biotin** constructs as replacements for wild-type streptavidin and **biotin** used in pretargeting and clin. diagnostics. **Biotin** dimers were engineered with certain parameters including water solubility, biotinidase resistance, and linker lengths long enough to span the distance between two **biotin**-binding sites of streptavidin. The bivalent **biotins** were compared to **biotin** in exchange, retention, and off-rate assays. The faster off-rate of SAv-Y43A allowed efficient exchange of prebound **biotin** by the **biotin** dimers. In fluorescent competition expts., the **biotin** dimer ligands displayed high avidity binding and essentially irreversible retention with SAv-Y43A. The off-rate of a biotinidase-stabilized **biotin** dimer from SAv-Y43A was 4.36 + 10-6 s-1, over 640 times slower compared to **biotin**. These findings strongly suggest that employing a mutant streptavidin in concert with a bivalent **biotin** can mitigate the deleterious impact of endogenous **biotin**, by allowing exchange of bound **biotin** and retention of the **biotin** dimer carriers.
REFERENCE COUNT: 41 THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L21 ANSWER 4 OF 16 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2001:923565 CAPLUS
DOCUMENT NUMBER: 136:42919
TITLE: **Biotin** derivatives for an extracorporeal device
INVENTOR(S): Sandberg, Bengt; Wilbur, Scott; Nilsson, Rune
PATENT ASSIGNEE(S): Mitra Medical Technology AB, Swed.; University of Washington
SOURCE: PCT Int. Appl., 45 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent

LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001095857	A2	20011220	WO 2001-SE1374	20010618
WO 2001095857	A3	20020328		
W: AE, AG, AL, AM, AT, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EC, EE, EE, ES, FI, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 2002159994	A1	20021031	US 2001-881213	20010615
CA 2412495	AA	20011220	CA 2001-2412495	20010618
AU 2001074761	A5	20011224	AU 2001-74761	20010618
EP 1289563	A2	20030312	EP 2001-941404	20010618
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
BR 2001011726	A	20030527	BR 2001-11726	20010618
JP 2004503299	T2	20040205	JP 2002-510039	20010618
NO 2002005931	A	20030214	NO 2002-5931	20021211
US 2004052784	A1	20040318	US 2003-311150	20030423

PRIORITY APPLN. INFO.:			
	SE 2000-2287	A	20000616
	US 2000-216625P	P	20000707
	WO 2001-SE1374	W	20010618

AB A method for the conditioning of an extracorporeal device is described, as well as a method for extracorporeal extraction of toxic material from mammalian body fluids in connection with diagnosis or treatment of a mammalian condition or disease. The methods comprise (i) a solution containing a reagent comprising **biotin** moieties, such as natural **biotin** or its derivs., and a toxin-binding moiety, (ii) linkers and a trifunctional crosslinking moiety, and (ii) an extracorporeal device comprising said reagent. For example, a dibiotin compound, 1-isothiocyanato-3,5-bis-(13'-biotinamidyl-4',7',10'-trioxatridecanamidyl)-aminoisophthalate was prepared and conjugated with a toxin-binding mol., i.e., monoclonal antibody 53-6A2. A dibiotin-toxin-binding conjugate was used for conditioning of an avidin-agarose column suitable for removal of toxins from blood.

L21 ANSWER 5 OF 16 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1999:668186 CAPLUS
DOCUMENT NUMBER: 132:46430
TITLE: Molecular Necklaces. Cross-Linking Hemoglobin with Reagents Containing Covalently Attached Ligands
AUTHOR(S): Crapatureanu, Sanda; Serbanescu, Ruxandra; Brevitt, Sharon Bisley; Kluger, Ronald
CORPORATE SOURCE: Lash Miller Laboratories Department of Chemistry, University of Toronto, Toronto, ON, M5S 3H6, Can.
SOURCE: Bioconjugate Chemistry (1999), 10(6), 1058-1067
CODEN: BCCHES; ISSN: 1043-1802
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 132:46430

AB Hb can be cross-linked and converted to a bioconjugate in one step by a mol. necklace, a reagent that contains two reacting sites and a pendant ligand. The compound to be conjugated is activated as an electrophile. The activated material is then combined with a reagent (3-aminoisophthalic acid) that contains a nucleophilic (amino) site and two latent (carboxyl)

sites. The latent sites of the product are activated as 3,5-dibromosalicylates to produce the cross-linker. Illustrative examples of crosslinking are presented with pendant **biotin** [bis(3,5-dibromosalicyl) N-biotinyl-5-aminoisophthalate] and pendant N-trifluoroacetyl-L-isoleucylglycine [bis(3,5-dibromosalicyl) N-(N-trifluoroacetyl-L-isoleucylglycyl)-5-aminoisophthalate]. The resulting modified Hbs contain two principal types of cross-link: (β-Lys-82-β'-Lys-82) and (α-Lys-99-α'-Lys-99). The functional properties of the modified Hb containing **biotin** in a (β-Lys-82-β'-Lys-82) cross-link are (pH 7.4, 55 μM heme, 25 °C, 0.1 M chloride, and 50 mM Bis-Tris) P50 = 4.9 Torr, n50 = 3.0, values which are approx. the same as for native Hb. The results of affinity chromatog. of the biotinylated cross-linked Hb using a column of immobilized avidin indicate that the pendant **biotin** is much less accessible than free **biotin**. We suggest that the results are consistent with the pendant species being strongly attracted into the Hb environment.

REFERENCE COUNT: 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L21 ANSWER 6 OF 16 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1999:325975 CAPLUS
DOCUMENT NUMBER: 130:357177
TITLE: Detoxication of active pharmaceutical substances using cyclodextrin oligomers
INVENTOR(S): Moser, Joerg G.
PATENT ASSIGNEE(S): Germany
SOURCE: PCT Int. Appl., 31 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 9924474	A1	19990520	WO 1998-EP7229		19981111
W: AL, AU, BA, BB, BG, BR, CA, CN, CU, CZ, EE, GE, HR, HU, ID, IL, IS, JP, KP, KR, LC, LK, LR, LS, LT, LV, MG, MK, MN, MX, NO, NZ, PL, RO, SG, SI, SK, SL, TR, TT, UA, US, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM					
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG					
AU 9916694	A1	19990531	AU 1999-16694		19981111
EP 1045863	A1	20001025	EP 1998-961184		19981111
EP 1045863	B1	20030402			
R: AT, BE, CH, DE, ES, FR, GB, IT, LI, NL					
JP 2001522901	T2	20011120	JP 2000-520482		19981111
AT 236195	E	20030415	AT 1998-961184		19981111
US 6642214	B1	20031104	US 2000-554223		20000803
PRIORITY APPLN. INFO.:			DE 1997-19749801	A	19971111
			DE 1998-19822416	A	19980519
			WO 1998-EP7229	W	19981111

AB Cyclodextrin oligomers with 2 cyclodextrins connected via a spacer B on the secondary side [CD-X-A-X-B-X-A-X-CD; CD = cyclodextrin; X = bond, NH, O, S, C(O); A = bond, C2-4 aliphatic residue; B = rigid, preferably hydrophilic residue] form strongly hydrophilic inclusion compds. with pharmaceutical agents and thereby prevent toxic side effects of drugs on nontarget cells by inhibiting their uptake into the cells. The drugs can be targeted to specific tissue sites by attachment of affinity groups such as antibodies to the cyclodextrin residues, and the drug can be released at the target site by destruction of the cyclodextrin residues (e.g. with cyclodextrinase from Klebsiella oxytoca). Provided the cyclodextrins are

connected on their secondary sides, their cavities will face each other; the distance between them is determined by the choice of spacer, and is preferably 0.8-1.8 nm. Thus, β-cyclodextrin was condensed with 4,4'-methylenebis(benzenesulfonyl chloride) and the product reacted with diaminopropane to form β-6(A-D)-diamidopropanediaminocyclodextrin (I). Sep., 2-monotosyl-β-cyclodextrin reacted with 3-mercaptopropionic acid to form β-(2)cyclodextrin-(3-thiopropionic acid) (II). Reaction of II with carbonyldiimidazole, N-hydroxysuccinimide, and a 2.5-fold molar excess of I produced a cyclodextrin trimer. Nude mice bearing OAT SCLC cell tumors were treated with biotinylated monoclonal antibody ICO 25 i.p., followed 24 h later by NeutrAvidin i.p., and after an addnl. 48 h by a biotinylcadaverine-labeled CD dimer-paclitaxel complex. Growth of the tumors was inhibited without occurrence of side effects.

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L21 ANSWER 7 OF 16 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1999:140535 CAPLUS
DOCUMENT NUMBER: 130:267698
TITLE: Synthesis of achiral linker reagents for direct labeling of oligonucleotides on solid supports
AUTHOR(S): Behrens, Carsten; Dahl, Otto
CORPORATE SOURCE: Department of Chemistry, University of Copenhagen, Copenhagen, DK-2100, Den.
SOURCE: Nucleosides & Nucleotides (1999), 18(2), 291-305
CODEN: NUNUD5; ISSN: 0732-8311
PUBLISHER: Marcel Dekker, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Full exptl. procedures for the synthesis of a series of new functional linker reagents and solid supports are reported. The achiral linker reagents and supports can be used for high yield incorporation of free amino groups, fluorescein or **biotin** into DNA oligomers.
REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L21 ANSWER 8 OF 16 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1999:109400 CAPLUS
DOCUMENT NUMBER: 130:177546
TITLE: Methods of receptor modulation and therapeutic and diagnostic uses therefor
INVENTOR(S): Morgan, A. Charles, Jr.; Wilbur, D. Scott
PATENT ASSIGNEE(S): Receptagen Corporation, USA; University of Washington
SOURCE: U.S., 47 pp., Cont.-in-part of U.S. Ser. No. 224,831, abandoned.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 6
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5869465	A	19990209	US 1995-406194	19950316
CA 2187346	AA	19951019	CA 1995-2187346	19950407
WO 9527723	A1	19951019	WO 1995-US4404	19950407
W: AU, CA, JP, KR, NO, NZ				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
AU 9522835	A1	19951030	AU 1995-22835	19950407
EP 754189	A1	19970122	EP 1995-916284	19950407
EP 754189	B1	20021009		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
JP 10502334	T2	19980303	JP 1995-526497	19950407

AT 225799	E	20021015	AT 1995-916284	19950407
US 5840712	A	19981124	US 1995-545151	19951019
US 6083926	A	20000704	US 1998-200422	19981123
PRIORITY APPLN. INFO.:			US 1994-224831	B2 19940408
			US 1995-406191	A 19950316
			US 1995-406192	A 19950316
			US 1995-406194	A 19950316
			WO 1995-US4404	W 19950407
			US 1995-545151	A3 19951019

AB Receptor-modulating agents capable of modulating cell surface receptors by affecting the cell-surface receptor trafficking pathway are utilized for the treatment and diagnosis of a variety of disorders in warm-blooded animals, including neoplastic disorders. The receptor-modulating agents are comprised of a covalently bound rerouting moiety and targeting moiety. Synthesis of several receptor-modulating agents using different functional classes of rerouting moieties is described. More specifically, a series of examples are presented which employ vitamin B12 as a targeting moiety in a receptor-modulating agent.

REFERENCE COUNT: 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L21 ANSWER 9 OF 16 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1998:776603 CAPLUS
DOCUMENT NUMBER: 130:38642
TITLE: Preparation of water soluble vitamin B12 as antiinflammatory receptor modulating agents
INVENTOR(S): Morgan, A. Charles, Jr.; Wilbur, D. Scott
PATENT ASSIGNEE(S): Receptagen Corporation, USA; University of Washington
SOURCE: U.S., 50 pp., Cont.-in-part of U.S. Ser. No. 224,831, abandoned.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 6
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5840880	A	19981124	US 1995-406191	19950316
CA 2187346	AA	19951019	CA 1995-2187346	19950407
WO 9527723	A1	19951019	WO 1995-US4404	19950407
W: AU, CA, JP, KR, NO, NZ				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
AU 9522835	A1	19951030	AU 1995-22835	19950407
EP 754189	A1	19970122	EP 1995-916284	19950407
EP 754189	B1	20021009		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
JP 10502334	T2	19980303	JP 1995-526497	19950407
AT 225799	E	20021015	AT 1995-916284	19950407
US 5840712	A	19981124	US 1995-545151	19951019
US 6083926	A	20000704	US 1998-200422	19981123
PRIORITY APPLN. INFO.:			US 1994-224831	B2 19940408
			US 1995-406191	A 19950316
			US 1995-406192	A 19950316
			US 1995-406194	A 19950316
			WO 1995-US4404	W 19950407
			US 1995-545151	A3 19951019

AB Vitamin B12 antiinflammatory receptor modulating agents capable of modulating cell surface receptors by affecting the cell surface receptor trafficking pathway are disclosed. The vitamin B12 receptor modulating agents are comprised of a covalently bound rerouting moiety and targeting moiety linked by a water-solubilizing linker. Synthesis of a vitamin B12/**biotin** conjugate and fusion protein receptor modulating agent is reported.

REFERENCE COUNT: 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L21 ANSWER 10 OF 16 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1998:776598 CAPLUS
DOCUMENT NUMBER: 130:38641
TITLE: Preparation of water soluble vitamin B12 as antiinflammatory receptor modulating agents
INVENTOR(S): Morgan, A. Charles, Jr.; Wilbur, D. Scott; Pathare, Pradip M.
PATENT ASSIGNEE(S): Receptagen Corporation, USA; University of Washington
SOURCE: U.S., 66 pp., Cont.-in-part of U.S. Ser. No. 406,191.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 6
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5840712	A	19981124	US 1995-545151	19951019
US 5739287	A	19980414	US 1995-406192	19950316
US 5840880	A	19981124	US 1995-406191	19950316
US 5869465	A	19990209	US 1995-406194	19950316
WO 9714711	A1	19970424	WO 1996-US16672	19961018
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG				
AU 9677182	A1	19970507	AU 1996-77182	19961018
EP 1015475	A1	20000705	EP 1996-940247	19961018
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
NZ 323127	A	20010330	NZ 1996-323127	19961018
US 6083926	A	20000704	US 1998-200422	19981123

PRIORITY APPLN. INFO.:		
US 1994-224831	B2	19940408
US 1995-406191	A2	19950316
US 1995-406192	A2	19950316
US 1995-406194	A2	19950316
WO 1995-US4404	A2	19950407
US 1995-545151	A	19951019
US 1995-545496	A	19951019
WO 1996-US16672	W	19961018

OTHER SOURCE(S): MARPAT 130:38641
AB Vitamin B12 antiinflammatory receptor modulating agents capable of modulating cell surface receptors by affecting the cell surface receptor trafficking pathway are disclosed. The vitamin B12 receptor modulating agents are comprised of a covalently bound rerouting moiety and targeting moiety linked by a water-solubilizing linker. Synthesis of a vitamin B12/**biotin** conjugate and fusion protein receptor modulating agent is reported.
REFERENCE COUNT: 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L21 ANSWER 11 OF 16 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1998:236288 CAPLUS
DOCUMENT NUMBER: 128:295003
TITLE: Preparation of biotinylated cobalamins as antiinflammatory agents and transcobalamin II receptors
INVENTOR(S): Wilbur, D. Scott; Pathare, Pradip M.; Morgan, A.

Charles, Jr.
PATENT ASSIGNEE(S): University of Washington, USA; Receptagen Corp.
SOURCE: U.S., 58 pp., Cont.-in-part of U.S. Ser. No. 224,831, abandoned.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 6
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5739287	A	19980414	US 1995-406192	19950316
CA 2187346	AA	19951019	CA 1995-2187346	19950407
WO 9527723	A1	19951019	WO 1995-US4404	19950407
W: AU, CA, JP, KR, NO, NZ				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
AU 9522835	A1	19951030	AU 1995-22835	19950407
EP 754189	A1	19970122	EP 1995-916284	19950407
EP 754189	B1	20021009		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
JP 10502334	T2	19980303	JP 1995-526497	19950407
AT 225799	E	20021015	AT 1995-916284	19950407
US 5840712	A	19981124	US 1995-545151	19951019
US 6083926	A	20000704	US 1998-200422	19981123

PRIORITY APPLN. INFO.:		
US 1994-224831	B2	19940408
US 1995-406191	A	19950316
US 1995-406192	A	19950316
US 1995-406194	A	19950316
WO 1995-US4404	W	19950407
US 1995-545151	A3	19951019

AB A biotinylated cobalamin, formed from a vitamin B12 mol. coupled to a **biotin** mol., is disclosed. In a preferred embodiment, the vitamin B12 mol. is cyanocobalamin. The **biotin** mol. can also be coupled to a rerouting moiety, optionally through a **biotin** binding protein such as avidin or streptavidin. The biotinylated cobalamin binds to a cell surface receptor, is invaginated, and once internalized affects the receptor trafficking pathway.
REFERENCE COUNT: 41 THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L21 ANSWER 12 OF 16 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1997:708440 CAPLUS
DOCUMENT NUMBER: 127:298612
TITLE: **Biotin** Reagents for Antibody Pretargeting. 2. Synthesis and in Vitro Evaluation of **Biotin** Dimers and Trimers for Crosslinking of Streptavidin
AUTHOR(S): Wilbur, D. Scott; Pathare, Pradip M.; Hamlin, Donald K.; Weerawarna, S. Ananda
CORPORATE SOURCE: Department of Radiation Oncology, University of Washington, Seattle, WA, 98195, USA
SOURCE: Bioconjugate Chemistry (1997), 8(6), 819-832
CODEN: BCCHES; ISSN: 1043-1802
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Polymerization and/or crosslinking of recombinant streptavidin (r-SAv) with **biotin** derivs. containing two **biotin** moieties (**biotin** dimers) or three **biotin** moieties (**biotin** trimers) has been investigated as a model for reagents to be used to increase the amount of radioactivity on cancer cells in tumor pretargeting protocols. In the investigation, six **biotin** dimers and three **biotin** trimers were synthesized. Most **biotin** derivs. synthesized had ether containing linker mols. incorporated to improve their

aqueous solubility The synthesized **biotin** dimers contained linker moieties which provided distances (when fully extended) of 13-49 Å between **biotin** carboxylate carbon atoms, and the **biotin** trimers contained linker moieties which provided distances of 31-53 Å between any two **biotin** carboxylate atoms. All of the **biotin** derivs. were evaluated for their ability to polymerize r-SAv in solution When the **biotin** derivs. were mixed with r-SAv, none of the **biotin** dimers caused polymerization, but all of the **biotin** trimers resulted in complete polymerization Some of the **biotin** dimers did cross-link r-SAv (to form r-SAv dimers, trimers, etc.), but the percentage of crosslinking was low (≤40%). The length of the linker mol. was important in crosslinking of **biotin** dimers. While linkers which provided distances of 13 and 19 Å between **biotin** carboxylate carbon atoms did not result in crosslinking, a linker which provided a 17 Å distance resulted in a small (≤10%) amount of crosslinking. Also, crosslinking was increased in **biotin** dimers with linkers which provided distances between **biotin** carboxylate carbon atoms of ≥23 Å. Crosslinking of streptavidin bound in polystyrene wells with **biotin** dimers and trimers was also examined In those expts., an excess of each **biotin** derivative was incubated at 37 °C for 10-30 min in polystyrene wells containing bound SAv. After the excess **biotin** derivative was rinsed from the wells, an excess of r-[125I]SAv was incubated for another 10-30 min. The amount of r-[125I]SAv bound after rinsing the excess from the wells was an indicator of the extent of crosslinking that occurred. The process of alternating addns. of reagents was repeated four times to demonstrate that bound radioactivity could be increased with each addition of [125I]SAv. The results of crosslinking r-SAv in polystyrene wells paralleled results from crosslinking in solution

L21 ANSWER 13 OF 16 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1997:377886 CAPLUS
DOCUMENT NUMBER: 126:343813
TITLE: Preparation of vitamin B12 receptor modulating agents
INVENTOR(S): Morgan, A. Charles, Jr.; Wilbur, D. Scott; Pathare, Pradip M.
PATENT ASSIGNEE(S): Receptagen Corporation, USA; University of Washington; Morgan, A. Charles, Jr.; Wilbur, D. Scott; Pathare, Pradip, M.
SOURCE: PCT Int. Appl., 97 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 6
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9714711	A1	19970424	WO 1996-US16672	19961018
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG				
US 5840712	A	19981124	US 1995-545151	19951019
AU 9677182	A1	19970507	AU 1996-77182	19961018
EP 1015475	A1	20000705	EP 1996-940247	19961018
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
NZ 323127	A	20010330	NZ 1996-323127	19961018
PRIORITY APPLN. INFO.:			US 1995-545151 A	19951019
			US 1995-545496 A	19951019

US 1994-224831	B2	19940408
US 1995-406191	A2	19950316
US 1995-406192	A2	19950316
US 1995-406194	A2	19950316
WO 1996-US16672	W	19961018

OTHER SOURCE(S): MARPAT 126:343813

AB Vitamin B12 receptor modulating agents capable of modulating cell surface receptors by affecting the cell surface receptor trafficking pathway are disclosed. The vitamin B12 receptor modulating agents are comprised of a covalently bound rerouting moiety and targeting moiety linked by a water-solubilizing linker.

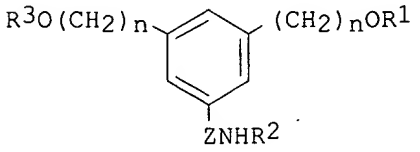
L21 ANSWER 14 OF 16 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1997:251007 CAPLUS
DOCUMENT NUMBER: 126:238622
TITLE: A new achiral linker reagent for the incorporation of multiple amino groups into oligonucleotides
INVENTOR(S): Behrens, Carsten; Petersen, Kenneth H.; Egholm, Michael; Nielsen, John; Dahl, Otto
PATENT ASSIGNEE(S): Behrens, Carsten, Den.; Petersen, Kenneth H.; Egholm, Michael; Nielsen, John; Dahl, Otto
SOURCE: PCT Int. Appl., 34 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9705156	A1	19970213	WO 1996-DK330	19960726
W: AL, AM, AT, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CU, CZ, CZ, DE, DE, DK, DK, EE, EE, ES, FI, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT				
AU 9665140	A1	19970226	AU 1996-65140	19960726

PRIORITY APPLN. INFO.:	DK 1995-863	A 19950727
	WO 1996-DK330	W 19960726

OTHER SOURCE(S): MARPAT 126:238622
GI



I

AB Functionalized achiral linker reagents, e.g. I [n = 1-3; Z = bond, C1-C10 chain optionally interrupted by 1-5 heteroatoms; R1 = H-phosphonate, phosphoramidite; R2 = amino protecting groups, e.g., PhCH2O2C, Me3CO2C, 9-fluorenylmethoxycarbonyl, allyloxycarbonyl, F3CCO, phthaloyl and reporter groups, e.g., fluorescein, dansyl, **biotin**, digoxigenin, N-oxyl-4,4-dimethyloxazolidine, N-oxyl-2,2,5,5-tetramethylpyrrolidine, texas red, tetramethylrhodamine, etc.; R3 = H, hydroxy protecting group, e.g., 4,4'-dimethoxytrityl, 9-fluorenylmethoxycarbonyl, etc.] were prepared and used to incorporate multiple primary amino groups or reporter groups into oligodeoxyribonucleotides following the phosphoramidite methodol. It is possible to substitute any deoxyribonucleotide, deoxynucleotide, or nucleotide with the linker in conventional phosphoramidite or

H-phosphonate DNA syntheses. Thus, the bis(hydroxymethyl)benzylamine I (Z = CH2; R1 = H; R2 = 9-fluorenylmethylcarbonyl; R3 = 4,4'-dimethoxytrityl; n = 1) was prepared from 5-nitroisophthalic acid in seven steps. Application of this reagent in standard solid-support phosphoramidite oligodeoxyribonucleotide preparation methodol. gave, e.g., 5'-GTAGATCACT-P(O)(OH)OCH2-X-CH2OH-3' [X = 1,3-(5-H2NCH2)C6H3] with 99.5% coupling efficiency.

L21 ANSWER 15 OF 16 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1997:155067 CAPLUS
DOCUMENT NUMBER: 126:207193
TITLE: Synthesis of Cobalamin Dimers Using Isophthalate Crosslinking of Corrin Ring Carboxylates and Evaluation of Their Binding to Transcobalamin. 2
AUTHOR(S): Pathare, Pradip M.; Wilbur, D. Scott; Hamlin, Donald K.; Heusser, Shannon; Quadros, Edward V.; McLoughlin, Patricia; Morgan, A. Charles
CORPORATE SOURCE: Department of Radiation Oncology, University of Washington, Seattle, WA, 98195, USA
SOURCE: Bioconjugate Chemistry (1997), 8(2), 161-172
CODEN: BCCHES; ISSN: 1043-1802
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Several cobalamin (Cbl) dimers have been prepared for evaluation as potential antiproliferative agents in the treatment of AIDS-related lymphoma. The Cbl dimers were synthesized by crosslinking Cbl carboxylates, produced by acid hydrolysis of the b-, d-, and e-propionamide side chains of cyanocobalamin (CN-Cbl), through an isophthalate mol. Linking mols. were used between the Cbl carboxylates and the isophthalate moiety. The linkers were incorporated to provide a distance between the two Cbl mols. such that the dimeric Cbls might bind two mols. of transcobalamin II (TCII), the Cbl transport protein in plasma. Initially, the linking moiety used was 1,12-diaminododecane, but the resulting dimers had low aqueous solubility To improve the solubility of the dimers, 4,7,10-trioxa-1,13-tridecanediamine was employed as the linking moiety. This improved the water solubility of the dimers considerably, while retaining the distance between the Cbl mols. at 41-42 Å (fully extended). To introduce addnl. substitution on Cbl dimers, 5-aminoisophthalic acid was used as the crosslinking reagent. P-Iodobenzoyl and p-(tri-n-butylstannyl)benzoyl conjugates of 5-aminoisophthalate were synthesized and used to prepare Cbl dimers. The stannylbenzoyl-conjugated Cbl dimers were prepared as precursors to be used in radioiodination reactions, and the iodobenzoyl-conjugated Cbl dimers were prepared as HPLC stds. for the radioiodinated product. Attempts to iodinate/radioiodinate the stannylbenzoyl Cbl dimers were unsuccessful. Although an explanation for this is not readily apparent, the failure to react may be due to the lipophilicity of the linker used and the steric environment of the two Cbl moieties. A biotinylated derivative of 5-aminoisophthalate was also synthesized and used to prepare biotinylated-Cbl dimers. In a competitive rhTCII binding assay with [57Co]CN-Cbl, Cbl dimers containing the lipophilic diaminododecane linking moiety had decreased binding avidities compared to those of Cbl monomers substituted at the same corrin ring carboxylate. However, Cbl dimers containing the water-solubilizing trioxadiamine linker appeared to have avidities similar to those of the Cbl monomers.
REFERENCE COUNT: 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L21 ANSWER 16 OF 16 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1986:626868 CAPLUS
DOCUMENT NUMBER: 105:226868
TITLE: Functionalized Keggin- and Dawson-type

cyclopentadienyltitanium heteropolytungstate anions: small, individually distinguishable labels for conventional transmission electron microscopy. 2. Reactions

AUTHOR(S): Keana, John F. W.; Ogan, Marc D.; Lu, Yixin; Beer, Michael; Varkey, J.

CORPORATE SOURCE: Dep. Chem., Univ. Oregon, Eugene, OR, 97403, USA

SOURCE: Journal of the American Chemical Society (1986), 108(25), 7957-63
CODEN: JACSAT; ISSN: 0002-7863

DOCUMENT TYPE: Journal

LANGUAGE: English

OTHER SOURCE(S): CASREACT 105:226868

GI For diagram(s), see printed CA Issue.

AB Cyclopentadienyltitanium substituted Keggin- and Dawson-type heteropolytungstate (HPT) anions, useful for labeling substrate mols. for visualization by conventional transmission electron microscopy, were functionalized by standard methods. Thus, Diels-Alder reaction of either Keggin HPT diene I or Dawson HPT diene II and N-phenylmaleimides gave protein-reactive compds., e.g., III. Also prepared were bromoacetamide, **biotin**, isothiocyanate, and N-hydroxysuccinimide ester derivs. Also prepared was IV containing two Dawson HPT units in close proximity. A HPT-labeled ATP derivative was also prepared The Keggin and Dawson HPT's were visible using conventional transmission electron microscopy. Their stability in the electron beam was high.

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                                                       ENTRY    SESSION
FULL ESTIMATED COST                                    78.61     234.62

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                                                       ENTRY    SESSION
CA SUBSCRIBER PRICE                                   -12.00     -12.00

FILE 'MEDLINE' ENTERED AT 14:09:19 ON 28 FEB 2006

FILE 'BIOSIS' ENTERED AT 14:09:19 ON 28 FEB 2006
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FILE 'EMBASE' ENTERED AT 14:09:19 ON 28 FEB 2006
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=> s triaminobenzene or tricarboxybenzene or dicarboxyaniline or diaminobenzoic acid
L22         242 TRIAMINOBENZENE OR TRICARBOXYBENZENE OR DICARBOXYANILINE OR
                DIAMINOBENZOIC ACID

=> d hist

     (FILE 'HOME' ENTERED AT 13:48:49 ON 28 FEB 2006)

     FILE 'REGISTRY' ENTERED AT 13:49:09 ON 28 FEB 2006
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L2            0 S TRICARBOXYBENZENE/CN
L3            7 S TRICARBOXYBENZENE
L4            3 S DICARBOXYANILINE
L5          652 S DIAMINOBENZOIC ACID
L6            1 S DIAMINOBENZOIC ACID/CN
L7            2 S 1,3,5-TRICARBOXYBENZENE
L8           13 S 1,3,5-TRIAMINOBENZENE
L9            1 S 3,5-ANILINE
L10           0 S 3,5-DIAMINOANILINE
L11           0 S 3,5-DIAMINO ANILINE
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L12           3 S DICARBOXYANILINE
L13         511 S 3,5-DIAMINOBENZOIC ACID
L14           1 S 3,5-DIAMINOBENZOIC ACID/CN
L15          13 S 1,3,5-TRIAMINOBENZENE
L16           1 S 1,3,5-TRIAMINOBENZENE/CN

     FILE 'CAPLUS' ENTERED AT 14:01:59 ON 28 FEB 2006
L17        1566 S 99-31-0/RN OR 554-95-0/RN OR 535-87-5/RN
L18         167 S 108-72-5/RN
L19        1670 S L17 OR L18
L20       29004 S BIOTIN OR NORBIOTIN OR HOMOBIOTIN OR OXYBIOTIN OR IMINOBIOTIN
L21          16 S L19 AND L20

     FILE 'MEDLINE, BIOSIS, EMBASE' ENTERED AT 14:09:19 ON 28 FEB 2006
L22         242 S TRIAMINOBENZENE OR TRICARBOXYBENZENE OR DICARBOXYANILINE OR D

=> s L20
L23      52577 L20

=> s L22 and L20
L24           0 L22 AND L20

=> s L22 and L23
L25           0 L22 AND L23

=> s L23 and benzene
L26          33 L23 AND BENZENE

=> s L26 and radionuclide
L27           0 L26 AND RADIONUCLIDE

=> s cancer or neoplasm
L28     3032102 CANCER OR NEOPLASM

=> s L26 and L28
L29           2 L26 AND L28

=> d 1-2 ibib abs

L29  ANSWER 1 OF 2     MEDLINE on STN
ACCESSION NUMBER:    1999034518     MEDLINE
DOCUMENT NUMBER:     PubMed ID: 9815170
TITLE:               Iodopyridine-for-iodobenzene substitution for use with low
                     molecular weight radiopharmaceuticals: application to
                     m-iodobenzylguanidine.
AUTHOR:              Vaidyanathan G; Zalutsky M R; DeGrado T R
CORPORATE SOURCE:    Department of Radiology, Duke University Medical Center,
                     P.O. Box 3808, Durham, North Carolina 27710, USA..
                     ganesan.v@duke.edu
CONTRACT NUMBER:     CA 60066 (NCI)
                     CA 74817 (NCI)
                     HL 54882 (NHLBI)
SOURCE:              Bioconjugate chemistry, (1998 Nov-Dec) Vol. 9, No. 6, pp.
                     758-64.
                     Journal code: 9010319. ISSN: 1043-1802.
PUB. COUNTRY:        United States
DOCUMENT TYPE:       Journal; Article; (JOURNAL ARTICLE)
LANGUAGE:            English
FILE SEGMENT:        Priority Journals
ENTRY MONTH:         199901
ENTRY DATE:          Entered STN: 19990202
                     Last Updated on STN: 19990202
                     Entered Medline: 19990119
AB   Substituting a pyridine ring for a benzene ring in the acylation
```

agent N-succinimidyl 3-iodobenzoate has resulted in a useful approach for the radiohalogenation of monoclonal antibodies, peptides, and labeled **biotin** conjugates. It was hypothesized that such a substitution in m-iodobenzylguanidine (MIBG), a radiotracer used in the detection and treatment of neuroendocrine tumors, might result in an analogue with more rapid normal tissue clearance, thereby facilitating its use for tumor therapy. For the preparation of this analogue, 3-guanidinomethyl-5-iodopyridine (GMIP; 9b), the silicon precursor 4 was synthesized starting from 5-bromonicotinic acid. Attempts to convert 4 to 9b under various conditions were not successful. Radioiodinated 9b could be prepared by the iododestannylation of the tin precursor 8 in 65-70% radiochemical yield. A number of in vitro, in vivo, and ex vivo studies showed that pyridine-for-**benzene** substitution in MIBG yielded a compound that no longer was taken up by the uptake-1 pathway.

L29 ANSWER 2 OF 2 EMBASE

ACCESSION NUMBER: 2004229695 EMBASE

TITLE: **Biotin** reagents in antibody pretargeting. 6. Synthesis and in vivo evaluation of astatinated and radioiodinated aryl- and nido-carboranyl-**biotin** derivatives.

AUTHOR: Wilbur D.S.; Hamlin D.K.; Chyan M.-K.; Kegley B.B.; Quinn J.; Vessella R.L.

CORPORATE SOURCE: D.S. Wilbur, Department of Radiation Oncology, University of Washington, 2121 N. 35th Street, Seattle, WA 98103-9103, United States. dswilbur@u.washington.edu

SOURCE: Bioconjugate Chemistry, (2004) Vol. 15, No. 3, pp. 601-616.
.
Refs: 57
ISSN: 1043-1802 CODEN: BCCHES

COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 016 Cancer
023 Nuclear Medicine
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 20040610
Last Updated on STN: 20040610

AB An investigation has been conducted to prepare and evaluate several radiohalogenated **biotin** derivatives as part of our studies to develop reagents for carrying (211)At in **cancer** pretargeting protocols. The primary goal of the investigation was to determine the in vivo stability and distribution properties of astatinated **biotin** derivatives. In addition to astatination, the **biotin** derivatives were radioiodinated for in vitro and in vivo comparison. Biodistributions were conducted in athymic mice, with sacrifice times of 1, 4, and 24 h to correspond to 9%, 32%, and 90% of (211)At decay (t(1/2) = 7.21 h). In the investigation, two **biotin** derivatives, 1a and 2a, were synthesized which had structures that contain a **biotin** moiety, a biotinidase-blocking moiety, an ether linker moiety, and an aryl stannane moiety for radiohalogenation. **Biotin** derivatives 1a and 2a were radiolabeled with (125/131)I to give [(125/131)I]1b or [(125)I]2b and with (211)At to give [(211)At]1c or [(211)At]2c. In vivo studies demonstrated that co-injected [(125)I]2b and [(131)I]1b had very similar tissue distributions in athymic mice. Co-injection of [(211)At]2c and [(125)I]2b provided data that indicated that rapid deastatination occurred in vivo. A second set of **biotin** derivatives, 3a, 4a, and 5a, were synthesized which had structures that contain a **biotin** moiety, a biotinidase-blocking moiety, and an anionic nido-carborane moiety for radiohalogenation. The **biotin** derivatives 4a and 5a contained an aryl moiety not present in 3a, and 5a had a trialkylamine functionality not present in 3a or 4a. **Biotin**

```
E1            3     WILBUER KLAUS/IN
E2            6     WILBUER KLAUS LEO/IN
E3            0 --> WILBUR/IN
E4            1     WILBUR ANDREW/IN
E5            4     WILBUR ARNOLD G/IN
E6            1     WILBUR ARTHUR LAZIER/IN
E7            6     WILBUR BENJAMIN C/IN
E8            1     WILBUR BENJAMIN C JR/IN
E9            1     WILBUR CLAYTON V/IN
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E11           1     WILBUR CLAYTON VANCE/IN
E12           7     WILBUR D S/IN
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L33           7 "WILBUR D S"/IN

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L33  ANSWER 1 OF 7  BIOSIS  COPYRIGHT (c) 2006 The Thomson Corporation  on STN
ACCESSION NUMBER:   2002:106487  BIOSIS
DOCUMENT NUMBER:    PREV200200106487
TITLE:              Biotinylated cobalamins.
AUTHOR(S):          Wilbur, D. S. [Inventor]; Pathare, P. M. [Inventor];
                    Morgan, C. A., Jr. [Inventor]
CORPORATE SOURCE:   Edmonds, Wash., USA
                    ASSIGNEE: RECEPTAGEN CORP.; UNIVERSITY OF WASHINGTON
PATENT INFORMATION: US 5739287 19980414
SOURCE:             Official Gazette of the United States Patent and Trademark
                    Office Patents, (April 14, 1998) Vol. 1209, No. 2, pp.
                    1477. print.
                    CODEN: OGUPE7. ISSN: 0098-1133.
DOCUMENT TYPE:      Patent
LANGUAGE:           English
ENTRY DATE:         Entered STN: 24 Jan 2002
                    Last Updated on STN: 25 Feb 2002

L33  ANSWER 2 OF 7  BIOSIS  COPYRIGHT (c) 2006 The Thomson Corporation  on STN
ACCESSION NUMBER:   2002:85153  BIOSIS
DOCUMENT NUMBER:    PREV200200085153
TITLE:              Iodinated borane cage molecules as X-ray contrast media.
AUTHOR(S):          Wilbur, D. S. [Inventor]
CORPORATE SOURCE:   Edmonds, Wash., USA
                    ASSIGNEE: UNIVERSITY OF WASHINGTON
PATENT INFORMATION: US 5679322 19971021
SOURCE:             Official Gazette of the United States Patent and Trademark
                    Office Patents, (Oct. 21, 1997) Vol. 1203, No. 3, pp. 2116.
                    print.
                    CODEN: OGUPE7. ISSN: 0098-1133.
DOCUMENT TYPE:      Patent
LANGUAGE:           English
ENTRY DATE:         Entered STN: 16 Jan 2002
                    Last Updated on STN: 25 Feb 2002

L33  ANSWER 3 OF 7  BIOSIS  COPYRIGHT (c) 2006 The Thomson Corporation  on STN
ACCESSION NUMBER:   2002:62459  BIOSIS
DOCUMENT NUMBER:    PREV200200062459
TITLE:              Radiohalogenated small molecules for protein labeling.
AUTHOR(S):          Wilbur, D. S. [Inventor]; Fritzberg, A. R. [Inventor]
CORPORATE SOURCE:   Edmonds, Wash., USA
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ASSIGNEE: NEORX CORPORATION
PATENT INFORMATION: US 5609848 19970311
SOURCE: Official Gazette of the United States Patent and Trademark Office Patents, (March 11, 1997) Vol. 1196, No. 2, pp. 1067. print.
CODEN: OGUPE7. ISSN: 0098-1133.
DOCUMENT TYPE: Patent
LANGUAGE: English
ENTRY DATE: Entered STN: 9 Jan 2002
Last Updated on STN: 25 Feb 2002

L33 ANSWER 4 OF 7 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN
ACCESSION NUMBER: 2002:34855 BIOSIS
DOCUMENT NUMBER: PREV200200034855
TITLE: Iodinated borane cage molecules as X-ray contrast media.
AUTHOR(S): Wilbur, D. S. [Inventor]
CORPORATE SOURCE: Edmonds, Wash., USA
ASSIGNEE: UNIVERSITY OF WASHINGTON
PATENT INFORMATION: US 5489673 19960206
SOURCE: Official Gazette of the United States Patent and Trademark Office Patents, (Feb. 6, 1996) Vol. 1183, No. 1, pp. 304. print.
CODEN: OGUPE7. ISSN: 0098-1133.
DOCUMENT TYPE: Patent
LANGUAGE: English
ENTRY DATE: Entered STN: 26 Dec 2001
Last Updated on STN: 25 Feb 2002

L33 ANSWER 5 OF 7 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN
ACCESSION NUMBER: 1999:246232 BIOSIS
DOCUMENT NUMBER: PREV199900246232
TITLE: Methods of receptor modulation and uses therefor.
AUTHOR(S): Morgan, A. C., Jr. [Inventor]; Wilbur, D. S. [Inventor]
CORPORATE SOURCE: Edmonds, Wash., USA
ASSIGNEE: RECEPTAGEN CORPORATION; UNIVERSITY OF WASHINGTON
PATENT INFORMATION: US 5869465 19990209
SOURCE: Official Gazette of the United States Patent and Trademark Office Patents, (Feb. 9, 1999) Vol. 1219, No. 2, pp. 1577. print.
CODEN: OGUPE7. ISSN: 0098-1133.
DOCUMENT TYPE: Patent
LANGUAGE: English
ENTRY DATE: Entered STN: 2 Jul 1999
Last Updated on STN: 2 Jul 1999

L33 ANSWER 6 OF 7 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN
ACCESSION NUMBER: 1999:71198 BIOSIS
DOCUMENT NUMBER: PREV199900071198
TITLE: Receptor modulating agents.
AUTHOR(S): Morgan, A. C., Jr. [Inventor]; Wilbur, D. S. [Inventor]
CORPORATE SOURCE: Edmonds, Wash., USA
ASSIGNEE: RECEPTAGEN CORPORATION; UNIVERSITY OF WASHINGTON
PATENT INFORMATION: US 5840880 19981124
SOURCE: Official Gazette of the United States Patent and Trademark Office Patents, (Nov. 24, 1998) Vol. 121, No. 4, pp. 4058. print.
CODEN: OGUPE7. ISSN: 0098-1133.
DOCUMENT TYPE: Patent
LANGUAGE: English
ENTRY DATE: Entered STN: 1 Mar 1999
Last Updated on STN: 1 Mar 1999

L33 ANSWER 7 OF 7 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN
ACCESSION NUMBER: 1999:71098 BIOSIS

DOCUMENT NUMBER: PREV199900071098
TITLE: Water soluble vitamin B-1-2 receptor modulating agents and methods related thereto.
AUTHOR(S): Morgan, A. C., Jr. [Inventor]; Wilbur, D. S. [Inventor]; Pathare, P. M. [Inventor]
CORPORATE SOURCE: Mill Creek, Wash., USA
ASSIGNEE: RECEPTAGEN CORPORATION; UNIVERSITY OF WA
PATENT INFORMATION: US 5840712 19981124
SOURCE: Official Gazette of the United States Patent and Trademark Office Patents, (Nov. 24, 1998) Vol. 121, No. 4, pp. 4011. print.
CODEN: OGUPE7. ISSN: 0098-1133.
DOCUMENT TYPE: Patent
LANGUAGE: English
ENTRY DATE: Entered STN: 1 Mar 1999
Last Updated on STN: 1 Mar 1999

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E1 1 SANDBERB F/AU
E2 1 SANDBERD M/AU
E3 1 --> SANDBERG/AU
E4 148 SANDBERG A/AU
E5 2095 SANDBERG A A/AU
E6 1 SANDBERG A ANDREN/AU
E7 3 SANDBERG A B/AU
E8 4 SANDBERG A C/AU
E9 6 SANDBERG A D/AU
E10 1 SANDBERG A E/AU
E11 177 SANDBERG A L/AU
E12 16 SANDBERG A M/AU

=> s e7
L34 3 "SANDBERG A B"/AU

=> d 1-3 ibib abs

L34 ANSWER 1 OF 3 MEDLINE on STN
ACCESSION NUMBER: 95231099 MEDLINE
DOCUMENT NUMBER: PubMed ID: 7715274
TITLE: [The physician-nurse cooperation is satisfactory]. Samarbetet lakare-sjukskoterskor gott.
AUTHOR: **Sandberg A B**
SOURCE: Lakartidningen, (1995 Apr 12) Vol. 92, No. 15, pp. 1563. Journal code: 0027707. ISSN: 0023-7205.
PUB. COUNTRY: Sweden
DOCUMENT TYPE: Letter
LANGUAGE: Swedish
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199505
ENTRY DATE: Entered STN: 19950524
Last Updated on STN: 19960129
Entered Medline: 19950518

L34 ANSWER 2 OF 3 MEDLINE on STN
ACCESSION NUMBER: 91155500 MEDLINE
DOCUMENT NUMBER: PubMed ID: 1999998
TITLE: [Changing of feeding schedules resulted in prolonged breast feeding period]. Omlagda matningsrutiner ledde till langre amningsperiod.
AUTHOR: **Sandberg A B**; Eriksson T; Marcusson E; Mjones S
CORPORATE SOURCE: Utredningssekreterare, Sundsvalls sjukhus.
SOURCE: Lakartidningen, (1991 Feb 13) Vol. 88, No. 7, pp. 497-8. Journal code: 0027707. ISSN: 0023-7205.